MEMORANDUM

SUBJECT: Dimethoate - Review of Pesticide Poisoning Incident Data

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The following data bases have been searched for the poisoning incident data on the active ingredient dimethoate (Case Number: 0088):

1) OPP Incident Data System (IDS) - reports of incidents from various sources, including registrants, other federal and state health and environmental agencies and individual consumers, submitted to OPP since 1992.

2) Poison Control Centers - as the result of Data-Call-Ins issued in 1993, OPP received Poison Control Center data covering the years 1985 through 1992 for 28 organophosphate and carbamate chemicals. Most of the national Poison Control Centers (PCCs) participate in a national data collection system, the Toxic Exposure Surveillance

System which obtains data from 70 centers at hospitals or universities. PCCs provide telephone consultation for individuals and health care providers on suspected poisonings, involving drugs, household products, pesticides, etc.

3) California Department of Food and Agriculture (replaced by the Department of Pesticide Regulation in 1991) - California has collected uniform data on suspected pesticide poisonings since 1982. Physicians are required, by statute, to report to their local health officer all occurrences of illness suspected of being related to exposure to pesticides. The majority of the incidents involve workers. Information on exposure (worker activity), type of illness (systemic, eye, skin, eye/skin and respiratory), likelihood of a causal relationship, and number of days off work and in hospital are provided.

4) National Pesticide Telecommunications Network (NPTN) - NPTN is a toll-free information service supported by OPP. A ranking of the top 200 active ingredients for which telephone calls were received during calendar years 1984-1991, inclusive has been prepared. The total number of calls was tabulated for the categories humans, animals, calls, incidents and others.

DIMETHOATE REVIEW

I. IDS

As of July 15, 1996, there were 23 reports involving dimethoate in IDS; 13 were received from California and may be included in the review of that data base. Nineteen (19) of the 23 reports involved 79 humans. Of the remaining 4 reports, 3 involved environmental/ ecological effects and 1 involved an unknown number of cattle.

II. Poison Control Center Data

Dimethoate was one of 28 chemicals for which Poison Control Center (PCC) data were requested. The following text and statistics are taken from an analysis of these data; see December 5, 1994 memo from Jerome Blondell to Joshua First.

The 28 chemicals were ranked using three types of measures: (A) number and percent occupational and non-occupational adult exposures reported to PCCs requiring treatment, hospitalization, displaying symptoms or serious life-threatening effects; (B) California data for handlers and field workers comparing number of agricultural poisonings to reported applications; and (C) ratios of poisonings and hospitalization for PCC cases to estimated pounds reported in agriculture for pesticides used primarily in agriculture.

A. Occupational and Non-occupational Exposure

There were a total of 697 cases in the PCC data base. Of these, 194 cases were occupational exposure; 120 (62%) involved exposure to dimethoate alone and 74 (38%) involved exposure to multiple chemicals, including dimethoate. There were a total of 503 adult non-occupational exposures; 424 (84%) involved this chemical alone and 79 (16%) were attributed to multiple chemicals.[1]

In this analysis, four measures of hazard were developed based on the Poison Control Center data, as listed below.

1. Percent of all accidental cases that were seen in or referred to a health care facility (HCF).

2. Percent of these cases (seen in or referred to HCF) that were admitted for medical care.

3. Percent of cases reporting symptoms based on just those cases where the medical outcome could be determined.

4. Percent of those cases that had a major medical outcome which could be defined as life-threatening or resulting in permanent disability.

Exposure to dimethoate alone or in combination with other chemicals was evaluated for each of these categories, giving a total of 8 measures. A ranking of the 28 chemicals was done based on these measures with the lowest number being the most frequently implicated in adverse effects. Table 1 presents the analyses for occupational and non-occupational exposures.

[1] Workers who were indirectly exposed (i.e. not handlers) were classified as non-occupational cases.

Table 1: Measures of Risk From Occupational and Non-occupational Exposure to Dimethoate Using Poison Control Center Data from 1985-1992[a]

	Occupational Exposure	Non-occupational Exposure
Percent Seen in HCF		
Single chemical exposure	69.2 (68.2)	38.9 (44.0)
Multiple chemical exposure	76.8 (69.8)	42.5 (46.1)
Percent Hospitalized		
Single chemical exposure	7.2 (12.2)	7.3 (9.9)
Multiple chemical exposure	10.1 (14.3)	8.9 (12.6)
Percent with Symptoms		
Single chemical exposure	86.4 (85.8)	73.9 (74.0)
Multiple chemical exposure	67.8 (85.8)	75.3 (75.2)
Percent with Life-threatening Symptoms		
Single chemical exposure	0.0 (0.0)	0.3^{*6} (0.0)
Multiple chemical exposure	0.7 (0.5)	0.5 (0.05)

a Extracted from Tables 2, 3, 5 and 6 in December 5, 1994 memo from Jerome Blondell to Joshua First; number in parentheses is median score for that category
* Top 25% of chemicals are ranked with a superscript of 1 to 7

As indicated in the above table, dimethoate ranked near the median of the 28 chemicals for all of the measures of risk, except for percent of cases with life-threatening symptoms. For this measure, it ranked number six in the list of the top seven most toxic chemicals when used alone. When used in combination with other chemicals, it also exceeded the median for this measure.

B. Ratios of poisoning - California Data

The incidence of **systemic poisoning cases** in agricultural workers reported to the California was compared to the number of applications of dimethoate. Those calculations, along with the median score for a total of 29 pesticides, are presented in Table 2 below.

Table 2: Systemic Poisonings/1,000 Applications in Selected Agricultural Workers Exposed to Dimethoate in California, 1982-1989[a]

Pesticide	Number of Appl.	Poisonings/1,000 Appl. (N) Primary Pesticide Only			Poisonings/1,000 Appl.(N) Multiple Pesticide Exposure		
		Handlers	Field Workers	Total	Handlers	Field Workers	Total
Dimethoate	93,254	.14 (13)	.28 (26)	.42 (39)	.38 (35)	.64 (60)	1.02 (95)
Median		.21	.20	.41	.44	.50	1.02

a Extracted from Table A5 in December 5, 1994 memo from Jerome Blondell to Joshua First; number in parentheses is the observed number of poisoned cases.

Dimethoate ranked higher than the median for field workers, whether used alone or in combination with other chemicals.

C. Ratios of Poisoning - U.S. Poison Control Data

Occupational ratio comparisons were limited to those pesticides used exclusively for agriculture for the review of the 28 chemicals. Since dimethoate also has non-agricultural uses, these comparisons were not made.

D. Exposure in Children

A separate analysis of the number of exposures in children five years of age and under from 1985-1992 was conducted. For dimethoate, there were 110 incidents; 96 (87%) involved exposure to dimethoate alone, while 14 (13%) involved exposure to a combination of chemicals, including dimethoate. These incidents were categorized using the four measures of hazard described above, as presented in Table 3.

Table 3: Measures of Risk in Children Exposed to Dimethoate as Compared to the Median of 17 Pesticides, Based on Poison Control Center Data, 1985-1992[a]

	Dimethoate Exposure		Median	
	Alone	In Combination	Alone	In Combination
Percent Seen in Health Care Facility	22.9	21.8	21.0	20.9
Percent Hospitalized	13.6	16.7	13.3	13.2
Percent of Cases with Symptoms	17.8	19.0	18.8	19.0

Percent of Cases with Life-threatening Symptoms	0.0	0.0	0.2	0.2

a Extracted from Tables A3 and A4 in December 5, 1994 memo from Jerome Blondell to Joshua First

As indicated in the above table, dimethoate's risk was comparable to the median for the 17 pesticides evaluated.

Ratios to compare the number of exposures, incidents and their severity to the amount of dimethoate used were computed using two different denominators, estimated number of containers in U.S. homes and estimated number of applications per year. The results are presented in Tables 4 and 5.

Table 4: Ratio of Dimethoate Childhood Exposures, Poisonings and Cases Seen in or Referred to Health Care Facilities (1985-1992) to Thousands of Products in U.S. Homes in 1990[a]

	Dimethoate	Median[b]
Exposures Per Use	.365	.492
Poisonings Per Use	0.50	.066
Health Care Referrals Per Use	0.80	.102

a Extracted from Table A6 in December 5, 1994 memo from Jerome Blondell to Joshua First
b Median of 10 carbamate and organophosphate pesticides

Table 5: Ratio of Dimethoate Childhood Exposures, Poisonings and Cases Seen in or Referred to Health Care Facilities to Thousands of Applications in U.S. Homes in 1990[a]

	Dimethoate	Median[b]
Exposures Per Use	.833*2	.162
Poisonings Per Use	.114*2	.018
Health Care Referrals Per Use	.182*2	.029

a Extracted from Table A7 in December 5, 1994 memo from Jerome Blondell to Joshua First
b Median of 10 carbamate and organophosphate pesticides
* Top 3 chemicals are ranked with superscript of 1 to 3

As indicated in the above tables, dimethoate ranked below the median in all measures when compared to thousands of products in U.S. homes, but well above the median when compared to thousands of applications in U.S. homes.

II. California Data - 1982 through 1993

Detailed descriptions of 493 cases submitted to the California Pesticide Illness Surveillance Program were reviewed. In 124 of these incidents, dimethoate was either used alone or in combination with other chemicals, but was judged to be responsible for the health effects.[2] (Only cases with a definite, probable or possible relationship were reviewed.) Table 6 presents the types of illness reported by year.

Table 6: Types of Illnesses Reported as a Result of Dimethoate Exposure in California, 1982-1993[a]

Year	No. of Cases	Illness Type			
		Systemic	Eye	Skin	Eye/Skin
1982	8	6	-	2	-
1983	15	10	3	2	-
1984	15	10	4	1	-
1985	6	4	1	-	1
1986	4	3	1	-	-
1987[b]	29	28	1	-	-
1988[c]	20	16	3	-	1
1989	9	8	1	3	-
1990	3	3	1	-	-
1991	11	11	4	-	-
1992	2	1	-	1	-
1993	2	-	1	1	-
Total	124	100	20	10	2

a Multiple illnesses may be reported for each case.
b Includes 23 airline employees who became ill after a bottle of dimethoate was broken in the airport terminal. All had at least one of the following symptoms: headache, nausea or lightheadedness.
c Includes 12 employees who experienced symptoms when exposed to dimethoate which had been applied outside by a ground maintenance crew. The air conditioner duct drew the pesticide odor into the building.

It should be noted that gastrointestinal symptoms (including

[2] There were 18 cases in which dimethoate was used in combination with other chemicals but was judged to be responsible for the illness. In 13 cases adjuvant was the other chemical, in 1 case each triadimefon or cryolite was involved, in 1 case triadimefon and *Bacillus thuringiensis* were involved, in 1 case propargite and mepiquat chloride and in the last case azinphos-methyl and chlorpyrifos.

nausea, vomiting, diarrhea, abdominal pain, etc.) were reported in 72 of the 100 who experienced systemic illnesses. The number of days disabled and hospitalized were also tabulated, as presented in Table 7 below.

Table 7: Number of Persons Disabled or Hospitalized for Indicated Number of Days after Dimethoate Exposure in California, 1982-1993

	Number of Persons Disabled	Number of Persons Hospitalized
One Day	11	2
Two Days	5	2
Three Days	5	1
Four Days	1	-
Five Days	2	-
Ten Days	2	-
More than 10 Days	1	-

The data were also tabulated by type of illnesses reported for individual activity categories; see Table 8 below.

Table 8: Illnesses by Activity Categories for Dimethoate Exposure in California, 1982-1993[a]

	Illness Category[b]				
Activity Category	Systemic	Eye	Skin	Eye/Skin	Total
Residue	43	3	4	-	50
Drift	32	7	3	-	42
Applicator	12	5	1	2	20
Other	11	1	-	-	12
Mixer/Loader	2	4	2	-	8
Total	100	20	10	2	132

a Residue = exposure to residual pesticide (field, structural, other); Drift = anyone exposed in the course of application who was not involved in making the application; termed as coincidental prior to 1989; Applicator = workers involved in all forms of pesticide applications (ground, hand, other); Other = all activity categories not otherwise identified; Mixer/Loader = mixes and loads pesticides;
b Multiple illnesses per case may be reported.

IV. NPTN

Dimethoate was number 29 on NPTN's list of the top 200 active ingredients for which calls were received from 1984 through 1991. A total of 565 calls involved 201 incidents in 129 humans, 13

animals and 59 others.

V. LITERATURE REPORTS OF HUMAN POISONINGS

Gallo and Lawryk report on several experimental studies in human volunteers. [1] For 21 days, one adult ingested dimethoate at a rate of 18 mg/day (≈ 0.26 mg/kg/day) and another at 9 mg/day; neither had any cholinesterase (ChE) inhibition. Twenty (20) adults ingested 2.5 mg/day (≈ 0.04 mg/kg/day) for 4 weeks with no toxic effects or inhibition of ChE. Twelve (12) persons who received 5 mg/day for 28 days and 9 who received 10 mg/day for 39 days showed no significant change in plasma or erythrocyte ChE. Eight (8) people who ingested 30 mg/day began to show a decrease in ChE activity by day 20; the depression lasted until the end of the study on day 57. Groups of 6 volunteers who received 45 and 60 mg/day had ChE depression earlier and to a greater degree; none had any clinical symptoms.

Multiple reports of suicide attempts by dimethoate ingestion are reported in the literature. Some of the cases may provide an approximation of the lethal dose in humans. A 52-year-old male ingested approximately 20 g of dimethoate (50 ml Roxion) and two hours later was comatosed with reduced reaction to painful stimuli.[2] Other clinical signs included muscular fasciculation, extreme miosis, hypersalivation and respiratory insufficiency. His plasma level of dimethoate was 34 µg/ml; the plasma ChE was unmeasurable. (It has been reported that the threshold plasma level of 0.01 µg/ml dimethoate is associated with cholinergic symptoms.) The patient responded to extensive treatment and was fully recovered 25 days after admission. Without treatment, he would have died most likely.

A 68-year-old male drank 3 ounces of concentrated Cygon 2-E (23.4% dimethoate).[3] He was immediately brought to the hospital and responded to standard treatment after having lost consciousness. However, within eight hours, he relapsed into a cholinergic crisis. Over the course of the next five weeks, he was maintained on an atropine drip and required a total dose of 30 grams, the largest amount ever reported to have been administered to a human at that time. The patient recovered completely except with a hearing deficit, nonspecific personality change and minimal spastic rigidity thought to be secondary to several anoxic episodes.

Dimethoate has been associated with the Intermediate Syndrome. This term was first used in 1987 to describe an organophosphate-related toxicity that is seen 24-96 hours after the acute cholinergic crisis. It is called intermediate because it occurs after the cholinergic crisis and before delayed neuropathy. The clinical syndrome is characterized by sudden respiratory paresis, weakness in the territory of multiple motor cranial nerves, weakness of neck flexor and proximal limb muscles and depressed tendon reflexes. In

a 3-year prospective study in Belgium, the frequency of the intermediate syndrome was determined in all patients admitted with acute organophosphate anticholinesterase poisoning.[4] Eight (8) of 19 patients developed intermediate syndrome. Agents which were determined to carry a high risk were methyl- and ethyl-parathion, fenthion and dimethoate. However, it was concluded that the intermediate syndrome was associated with prolonged acetylcholinesterase inhibition, rather than the toxicant involved.

Gallo and Lawryk report that dimethoate itself has not been an important cause of irritation.[1] However, severe irritation of the eyes occurred in workers who manufactured the chemical. During the neutralization of the acid intermediate, some of the molecules combined to form bis(dimethoxythiophosphoryl) disulfide. Both of these compounds are irritating in laboratory animal studies.

V. SUMMARY/CONCLUSIONS

IDS

As of July 15, 1996, there were 23 reports involving dimethoate in IDS; 13 were received from California and may be included in the review of that data base. Nineteen (19) of the 23 reports involved 79 humans. Of the remaining 4 reports, 3 involved environmental/ ecological effects and 1 involved an unknown number of cattle.

POISON CONTROL CENTER

Dimethoate was one of 28 chemicals for which Poison Control Center (PCC) data were requested under a Data-Call-In issued in 1993. There were a total of 697 cases involving dimethoate in the PCC data base from 1985 through 1992. Of these, 194 cases were occupational exposure; 120 (62%) involved exposure to dimethoate alone and 74 (38%) involved exposure to multiple chemicals, including dimethoate. There were a total of 503 adult non-occupational exposures; 424 (84%) involved this chemical alone and 79 (16%) were attributed to multiple chemicals. For the analysis of this data, four measures of hazard were developed, as listed below.

1. Percent of all accidental cases that were seen in or referred to a health care facility (HCF).

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3. Percent of cases reporting symptoms based on just those cases where the medical outcome could be determined.

4. Percent of those cases that had a major medical outcome which

could be defined as life-threatening or resulting in permanent disability.

Dimethoate ranked near the median for the 28 chemicals for all measures, whether used alone or in combination with other chemicals.

Another measure of risk which was used in this analysis was the ratio of systemic poisonings (in agricultural workers in California) per 1,000 applications of pesticide. Dimethoate ranked lower than the median for handlers but above the median for field workers, whether used alone or in combination with other chemicals.

A separate analysis was performed for exposures of children five years of age and under. For dimethoate, there were 110 incidents; 96 (87%) involved exposure to dimethoate alone, while 14 (13%) involved exposure to a combination of chemicals, including dimethoate. Using the same four measures of hazard as described above, dimethoate was comparable to the median of 17 pesticides.

The PCC data in children exposed to dimethoate were used to compare incidents to the amount of the chemical in U.S. homes in 1990, using both number of containers and number of applications as denominators. When using number of applications, dimethoate was number two in a ranking of the top three (of 10) chemicals when evaluating exposures per use, poisonings per use and health care referrals per use.

CALIFORNIA DATA, 1982-1993

Detailed descriptions of 493 cases submitted to the California Pesticide Illness Surveillance Program were reviewed. In 124 of these incidents, dimethoate was either used alone or in combination with other chemicals, but was judged to be responsible for the health effects. (Only cases with a definite, probable or possible relationship were reviewed.) The vast majority of the cases involved symptoms of systemic illness; gastrointestinal symptoms were reported in 72% of the 124 cases. Disability ranging from one to more than 10 days was reported in 27 of these cases; five persons were hospitalized. The activity categories most often associated with reports of illness were exposure to residual pesticide (during field, structural or other application) and drift (anyone exposed during course of application who was not involved in making the application).

NPTN

Dimethoate was number 29 on NPTN's list of the top 200 active ingredients for which calls were received from 1984 through 1991.

A total of 565 calls involved 201 incidents in 129 humans, 13 animals and 59 others.

VI. RECOMMENDATIONS

1. Risk mitigation measures for dimethoate for agricultural workers should be in accordance with the Acute Worker Risk Strategy.

2. From review of the Poison Control Center Data, it appears that children exposed to dimethoate in the home are at risk for poisoning. Household products should be scrutinized for risk mitigation measures to reduce this exposure.

3. From the review of the California data, it appears that mild to moderate symptoms of dimethoate poisoning can occur in persons not directly involved in pesticide application. Risk mitigation measures should reduce possible dimethoate exposure via drift and contact with residual chemical.

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